FOUR CASES WITH PULMONARY ALVEOLAR PROTEINOSIS

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Pulmonary alveolar proteinosis is described in 1958 by Rosen, Castelman and Liebow against the background of experience had with clinical, biopsy and autopsy material, obtained from 27 patients. Since then up to the end of 1964, more than 60 case reports have been made with varying clinical, roentgenological and morphological characteristic features (3).

It concerns a chronic affection of the lungs, characterized by filling up the distal air sacs — alveoli and bronchioles — of granular and fibrous protein substances, containing PAS positive matter, occasionally mixed up with lipids (1), without inflammatory alterations.

Its clinical manifestations are different — in the early phases the course is asymptomatic, whereas in advanced forms the condition accounts for prolonged periods of dyspnea, coughing and paucity of sputum. Usually it runs a course of slow and protracted evolution.

Diagnosis is impossible without morphological investigation. The cases hitherto reported in literature have been diagnosed exclusively on the basis of histological and histochemical investigations of biopsy material or post mortem (5). This is the only way possible providing for differentiation of pulmonary proteinosis from pulmonary edema, cholesterol pneumonia, pneumocystic pneumonia, sarcoidosis etc.

The disease is of unknown etiology and pathogenesis. The latter fact is confirmed by the great number of theories suggested: the material filling up the alveoli and bronchioles originates from proliferated septal cells (1), subsequent to severe pulmonary congestion (2), subsequent to alveolar cells' degeneration (3, 6), due to pulmonary infection, congenital or acquired defect of pulmonary capillaries etc.

The first case report in Bulgarian medical literature was made by B. Konstantinov in 1963.

At the Chair of Pathoanatomy of the Higher Medical Institute — Varna, over a period of four years, diagnosis alveolar proteinosis was established as a concomitant affection in four patients.

Case I — S. P. K., male aged 74, pensioner, treated at the Surgical Dept. of the District Hospital in Varna; history of illness № 2737/1963. He was admitted as an emergency case for burns of the left leg. Following two-week hospitalization he died. Referred for autopsy with diagnosis: second degree burn injury of the left leg; generalised arteriosclerosis. During post mortem examination (autopsy report № 134/1963), in addition to burns, also evidence for hypertension with alterations of the organs and chronic cardiac insufficiency were established.

Case II — P. H. F., male aged 78, pensioner, treated at the United City Hospital — Byala, with lethal outcome. The material obtained at autopsy was referred for examination with diagnosis: sclerosis of myocardium; cardiac insufficiency I—II degree. The morphological investigation of the material (biopsy № 1202/13. V. 1963) proved infarction of the myocardium in process of organization and evidence for chronic cardiac insufficiency.

Case III — Z. R. K., female aged 67, pensioner, treated at the clinic of infectious diseases of the Higher Medical Institute — Varna; history of illness № 1958/1964. She fell ill two months prior to admission at the clinic with the following complaints: loss of weight, listless and icteric tinge of the sclera and skin. The condition gradually deteriorated and regardless of treatment undertaken, after a 20-day hospitalization she died. The body was referred for autopsy with the following definitive diagnosis: obstructive jaundice; sclerosis of the myocardium, rightside bronchopneumonia and acute cardiovascular insufficiency. The autopsy revealed (autopsy report № 354/1964): subacute toxic hepatic dystrophy, universal icterus and bronchopneumonia in the right lung.

Case IV — E. A. G., female aged 70 years, treated at the Internal Disease Dept. of the Naval Hospital — Varna (history of illness № 2607/1964). Since nearly 10 years she complains of easy fatigability and suffers of asthma (short breath). Treatment was carried out in the department for one week with lethal outcome. The body was sent for autopsy with diagnosis: atherosclerotic myocardiosclerosis; cardiac insufficiency II—III degree; intestinal carcinoma with metastasis in the omentum; chronic bronchitis, pulmonary emphysema and diabetes mellitus. The autopsy disclosed (autopsy report № 726/1964) carcinoma of the stomach, metastases in the regional lymph nodes; sclerosis of myocardium; senile emphysema and lipomatosis of the pancreas.

The similarities of the clinical manifestations and pathoanatomical findings of the four cases herein presented justify their parallel consideration.

The prolonged past history of cardiac and pulmonary insufficiency, manifested in varying degrees, is characteristic for all the patients. The X-ray investigations did not provide data doubtful for alveolar proteinosis. Investigations of blood proteins were not carried out. The autopsy established reduced elasticity of the lungs in all patients. In two of them (autopsy report № 134 and biopsy № 1202/1963) the lungs did not show uniformly indurated consistency and cutting them with a scalpel was rather difficult. The histological study revealed areas of thickened alveolar walls, due to fibrous processes. Aponeurotic bands of collagen connective tissue were found around the bronchi and major blood vessels. In other areas some of the alveoli were greatly expanded, unequal in size with thinned and ruptured walls, whereas others were atelectatic. The remainder two cases exhibited the classical picture of chronic emphysema.

The blood vessels were with preserved histological structure and reduced elastic fibers.

The characteristic feature in the pulmonary finding which attracted our attention in particular, was that in some of the alveoli irregularly roundish, pale rose-stained corpuscles were found, freely lying in their lumen. On weaker magnification they seemed homogenous, devoid of proper structure and in most of them a darker stained center was disclosed (Fig. 1), very likely due

to desquamated epithelial cells and dust. On great magnification it is clearly seen that the matter they are composed of is either finely granular or fibrous and their structure is concentric-lamellar (Fig. 2) or striped-radial (Fig. 3).

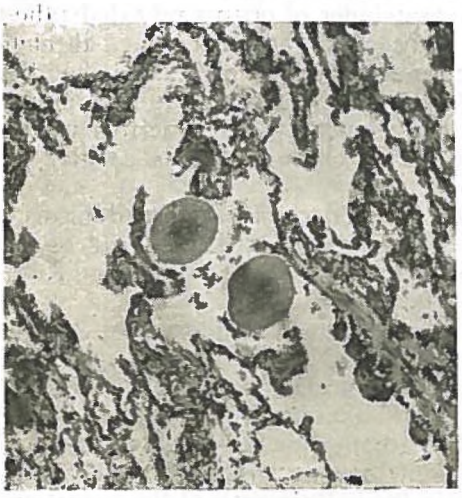

Fig. 1

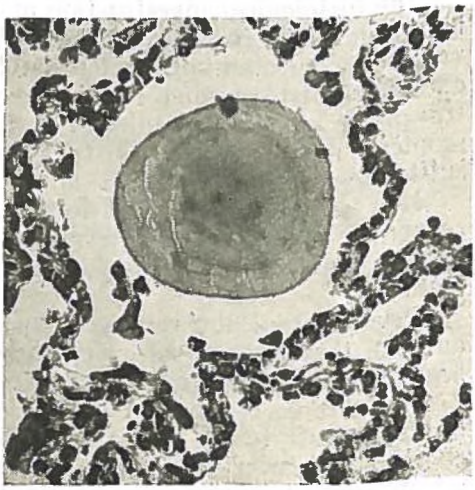

Fig. 2

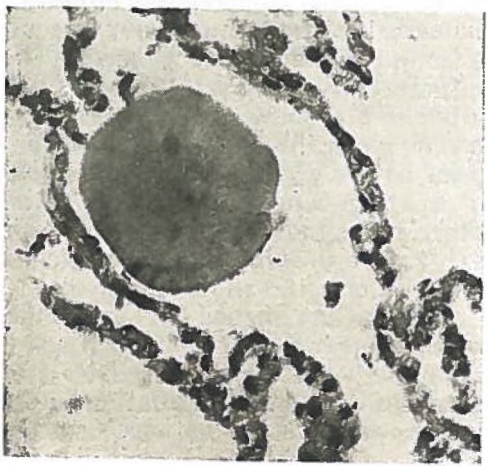

Fig. 3

The latter finding is similar to the finding in pulmonary alveolar microlithiasis. The histochemical investigations however, show that in the formations described calcium salts are not found — an unquestionable sign of microlithiasis. The substance these corpuscles are made of is PAS positive and displays a slight metachromasia. All these findings justified the assumption that in this case mucoproteid complexes are concerned. Along

with these complexes, single desquamated epithelial cells, siderophages and lipophages are likewise found within their alveoli. Signs of inflammation are not encountered. Isolated siderophages, lipophages, septal cells and lymphoid elements are found within the intraalveolar barriers.

The histological investigation of the remainder of organs revealed rather more significant changes involving the myocardium and manifested through vascularly substantiated sclerosis. Secure data were also established for chronic rightside cardiac insufficiency (myristica liver and cyanotic induratins of the kidneys and spleen). It should be emphasized that neither macroscopical, not pronounced histological data for chronic leftside cardiac insufficiency were found.

It is accepted that in all four cases a pulmonary alveolar proteinosis is concerned in one of its late stages of development, when shaping of the corpora amylacea takes place, to use the term coined by Anderson and Kaufmann.

Regardless of the relatively small number of cases diagnosed by the authors, they provide sufficient ground for elucidation of the interrelationships existing between pulmonary alveolar proteinosis and microlithiasis.

The chronic myocardial lesions led by all likelihood to a certain degree of blood stasis in the lungs, insufficient to account for heavy morphological changes, but nevertheless perfectly sufficient to cause vascular permeability, which, very likely plays an essential role in the pathogenesis of the condition. The latter supposition is in conformity with concepts expressed by other authors (2, 3, 6) insofar it concerns a transudate, primarily accounting for passive filling up of the alveoli, composed of proteids, lipids and variable number of desquamated cells. Hardly, anywuy, vascular permeability could be accepted as the unique pathological moment. The high incidence of chronic cardiac insufficiency is universally proved, and accordingly — the low incidence of pulmonary proteinosis, in spite of directed investigations carried out by numerous medical workers. For the time being it is difficult to determine the exact nature of concurrent etiopathogenetic factors.

The relationship existing between pulmonary alveolar proteinosis and microlithiasis is rather more thoroughly elucidated by the review of our series. Many writers (1, 2, 3, 4, 5) state, that the original matter in proteinosis undergoes a variable evolution: „it is subject to necrosis", „it becomes denser" wherefrom corpora amylacea are shaped out etc. On the other hand, bearing in mind that the protein framework of this matter lies at the base of the microliths, on which calcium carbonates and phosphates are deposited (1, 2), we think that the cases herein described represent an intermediate stage of one and the same disease appearing under various forms (proteinosis or microlithiasis).

In accordance with the literature survey and experience gained, it is assumed for possible that pulmonary alveolar proteinosis is manifested also as a syndrome, characteristic for other morbid conditions. The solution of the latter and a number of other obscure problems related to proteinosis implies a correctly directed research work and thorough investigation of all patients observed as well as their prompt report in the relevant literature.

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СЛУЧАЙ С ЛЕГОЧНЫМ АЛЬВЕОЛЯРНЫМ ПРОТЕИНОЗОМ

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РЕЗЮМЕ

Сообщаются четыре случая с легочным альвеолярным протеинозом, доказанным морфологически как сопутствующее заболевание. Находка соответствует описанным некоторым авторами corpora amylacea, которые являются основой легочного микролитиаза. Это позволяет предположить, что легочный альвеолярный протеиноз и микролитиаз являются разными стадиями одного и того-же заболевания. Наблюдаемые больные умерли в результате разных основных заболеваний и поэтому допускается возможность, что легочный протеиноз является и как синдром других заболеваний.